



Armed Forces College of Medicine AFCM



Diuretics (3)

By

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INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Identify different members of diuretics
2. Explain the mechanism of action of different diuretics
3. Relate the mechanism of action of diuretics to their clinical use
4. Explain the adverse effects of carbonic anhydrase inhibitors and potassium sparing diuretics and osmotic diuretics.



Potassium Retaining Diuretics

Mechanism

- Inhibit $\text{Na}^+/\text{K}^+/\text{H}^+$ exchange at the distal tubule by two different mechanisms:

I. Indirect: Spironolactone & eplerenone (delayed onset of action)

Antagonize aldosterone receptor-binding resulting in decreased synthesis of a specific protein that stimulates the Na^+ pump (requires 3 - 4 days).

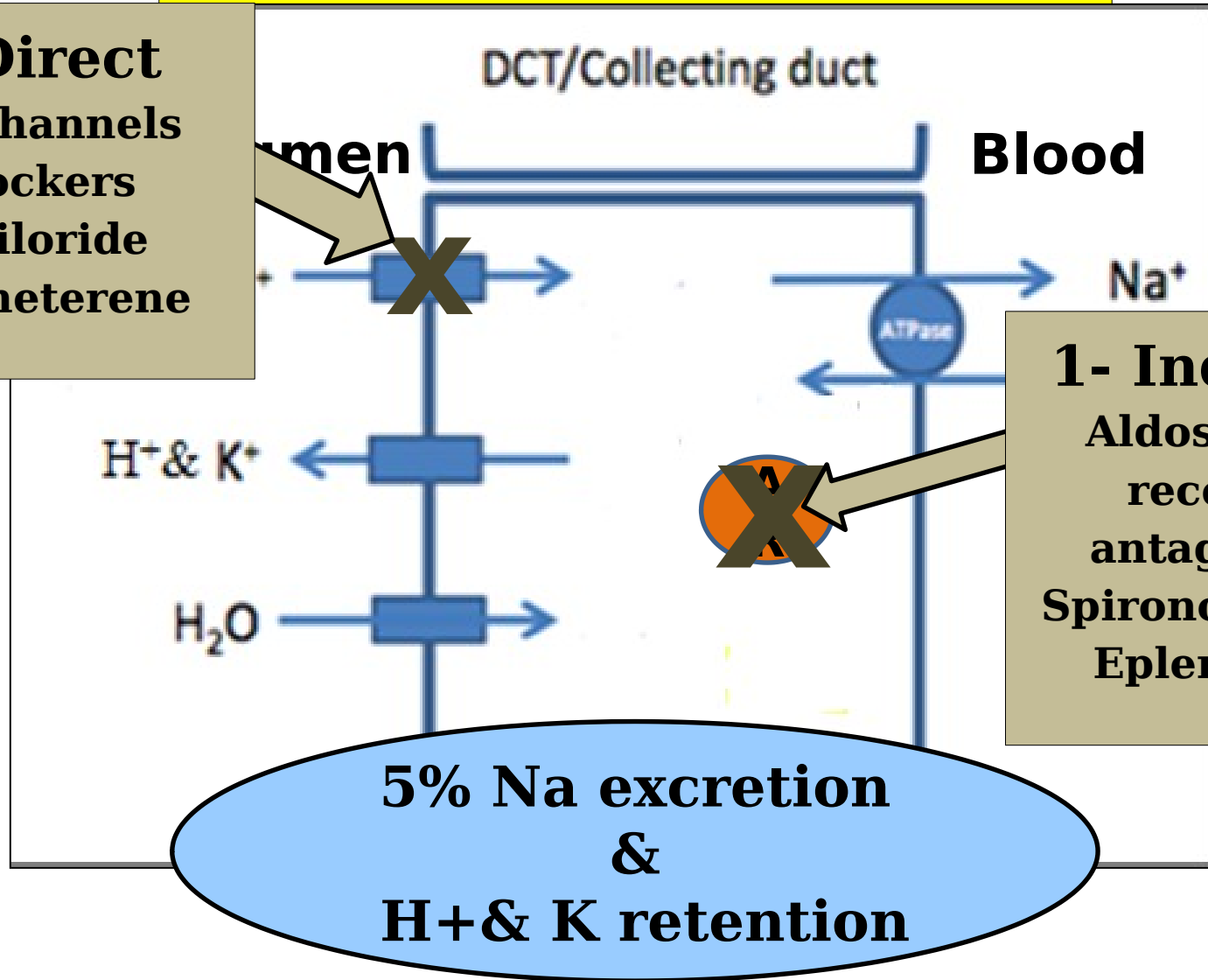
II. Direct: Triamterene & amiloride (rapid onset of action)

Act independent of aldosterone → block Na^+ channels directly.



Potassium Retaining Diuretics

**2- Direct
Na Channels
Blockers
Amiloride
Triameterene**



**1- Indirect
Aldosterone
receptor
antagonists
Spironolactone
Eplerenone**



Potassium Retaining Diuretics

Edema of hyperaldosteronism (liver cirrhosis, nephrotic syndrome & CHF) is resistant to other diuretics since Na^+ lost by other diuretics is reabsorbed again by excess aldosterone at $\text{Na}^+/\text{K}^+/\text{H}^+$ exchange site in distal tubule (also directly acting K^+ -retaining diuretics are less effective than spironolactone in hyperaldosteronism).

Triamterene and amiloride, are preferable to spironolactone as they are more rapid & shorter acting → daily dosage adjustment possible.

They are combined with K^+ -losing diuretics (loop & thiazide diuretics) to potentiate their diuretic effect & to antagonize their hypokalemic effect (more effective than exogenous K^+ & Mg^{++} supplements).



Potassium Retaining Diuretics

Adverse Effects

1. $\uparrow K^+$
 2. $\uparrow H^+$
- Drugs (β Bs - NSAIDs- ACEIs - ARBs) & Renal impairment

3. Gynecomastia



OSMOTIC DIURETICS

Mechanism of Action

Mannitol is freely filtrated at the glomerulus with limited reabsorption by renal tubules resulting in: Increase in osmotic pressure of tubular filtrate with retention of water and increased urine volume (main effect → useful as dehydrating agents).



OSMOTIC DIURETICS

(MANNITOL) (Powerful diuretic action)

uses

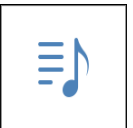
- 1. Cerebral edema**
- 2. Acute congestive glaucoma.**
- 3. Prophylaxis against acute renal failure**

Mannitol prevents acute renal failure following surgery, trauma or hemolytic transfusion reactions by maintaining high rate of urine flow, preventing concentration of toxic agents which cause renal damage.



Adverse Effects & Contraindications

In impaired renal function (e.g. acute renal failure), mannitol is not filtered & persists in plasma → ↑ intravascular volume → heart failure & dilutional hyponatremia → **contraindicated in acute renal failure & congestive heart failure.**



Carbonic Anhydrase Inhibitors (CAIs)

Acetazolamide- Dorzolamide - brinzolamide

Mechanism of Action

Inhibit carbonic anhydrase enzyme responsible for H^+ production $\rightarrow$ inhibition of Na^+/H^+ exchange at the proximal tubules $\rightarrow$ inhibition of NaHCO_3 reabsorption $\rightarrow$ loss of NaHCO_3 in urine leading to:

- a.** Diuresis with alkaline urine.
- b.** Decreased blood bicarbonate with metabolic acidosis.



Carbonic Anhydrase Inhibitors (CAIS)

**Acetazolamide- Dorzolamide -
brinzolamide**

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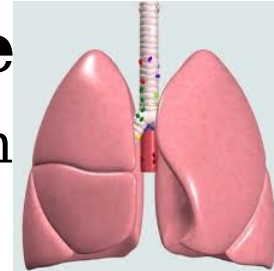
Carbonic anhydrase inhibitors (CAIS)

Acetazolamide- Dorzolamide -

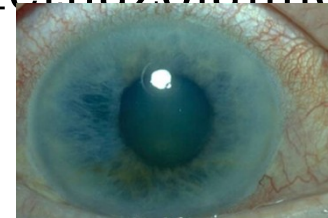
Indications (4 Es) **brinzolamide**

1. Emphysema and high altitude sickn

2. Epilepsy



3. Eye: treatment of glaucoma (oral Methazolamide or topical Dorzolamide & Brinzolamide)



4. Excretion of acidic toxins

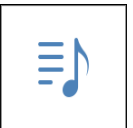
Adverse Reactions

1. Drowsiness 2. Calcium and phosphate

3. Hypersensitivity reactions
stones



Lecture quiz



If you prescribed, frusemide, spironolactone, acetazolamide, hydrochlorothiazide to your patients, choose the possible diuretic that can produce these specific adverse effects

Which one can predispose to:

1. Impaired glucose tolerance

hydrochlorothiazide

2. Ototoxicity

frusemide

3. Drowsiness

acetazolamide

.....

4. Gynecomastia

spironolactone



What are the expected drug interactions from the following combinations with diuretics?

1. loop with thiazide diuretic.....

hypokalemia
2. Cephalosporin with loop diuretics.....

Interstitial nephritis

Decrease efficacy of loop diuretics
3. NSAIDs with loop diuretics.....



SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.





Thank You